Please amend the above-identified application as follows:

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application.

Listing of Claims:

1-67. (Cancelled)

68. (previously presented): An isolated nucleic acid molecule comprising a regulatory sequence operably linked to a nucleic acid sequence that encodes an engineered ribonucleic acid (RNA) agent, wherein the agent comprises

(i) a first stem portion comprising a sequence of at least 18 nucleotides that is complementary to a sequence of a messenger RNA (mRNA) of a target gene;

(ii) a second stem portion comprising a sequence of at least 18 nucleotides that is sufficiently complementary to the first stem portion to hybridize with the first stem portion to form a duplex stem; and

(iii) a loop portion that connects the two stem portions.

69. (previously presented): The nucleic acid molecule of claim 68, wherein the first stem portion is fully complementary to the mRNA sequence.

70. (previously presented): The nucleic acid molecule of claim 68, wherein the second stem portion is fully so complementary to the first stem portion.

71. (previously presented): The nucleic acid molecule of claim 68, wherein the first stem portion is located at a 5′ end of the RNA agent.

72. (previously presented): The nucleic acid molecule of claim 68, wherein the first stem portion is located at a 3′ end of the RNA agent.

73. (previously presented): The nucleic acid molecule of claim 68, wherein the loop portion comprises at least 4 nucleotides.

74. (previously presented): The nucleic acid molecule of claim 68, wherein the loop portion comprises at least 7 nucleotides.

75. (previously presented): The nucleic acid molecule of claim 68, wherein the loop portion comprises 11 nucleotides.

76. (previously presented): The nucleic acid molecule of claim 68, wherein the sequence of the mRNA is located from 100 to 300 nucleotides 3′ of the start of translation of the mRNA.

77. (previously presented): The nucleic acid molecule of claim 68, wherein the sequence of the mRNA is located in a 5′ untranslated region (UTR) or a 3′ UTR of the mRNA.

78. (previously presented): The nucleic acid molecule of claim 68, wherein the first and second stem portions each comprise about 18 to about 30 nucleotides.

79. (previously presented): The nucleic acid molecule of claim 68, wherein the first and second stem portions each comprise about 22 to about 28 nucleotides.

80. (previously presented): The nucleic acid molecule of claim 68, wherein the first and second stem portions each comprise the same number of nucleotides.

81. (previously presented): The nucleic acid molecule of claim 68, wherein one of the first and second stem portions comprises 1 to 4 more nucleotides than the other stem portion.

82. (previously presented): The nucleic acid molecule of claim 68, wherein the regulatory sequence comprises a Pol III or Pol II promoter.

83. (previously presented): The nucleic acid molecule of claim 68, wherein the regulatory sequence is constitutive or inducible.

84. (previously presented): A vector comprising the nucleic acid molecule of claim 68.

85. (previously presented): The vector of claim 84, wherein the vector is a plasmid or a viral vector.

86. (previously presented): The vector of claim 85, wherein the viral vector is a retroviral vector.

87. (previously presented): A host cell containing the nucleic acid molecule of claim 68.

88. (previously presented): The host cell of claim 87, wherein the cell is a mammalian cell.

89. (previously presented): A transgene comprising the nucleic acid of claim 68.

90. (previously presented): An engineered RNA agent comprising

i) a first stem portion comprising a sequence of at least 18 nucleotides that is complementary to a sequence of a messenger RNA (mRNA) of a target gene;

ii)a second stem portion comprising a sequence of at least 18 nucleotides that is sufficiently complementary to the first stem portion to hybridize with the first stem portion to form a duplex stem; and

iii) a loop portion that connects the two stem portions.

91. (previously presented): The agent of claim 90, wherein the first stem portion is fully complementary to the mRNA sequence.

92. (previously presented): The agent of claim 90, wherein the second stem portion is fully complementary to the first stem portion.

93. (previously presented): The agent of claim 90, wherein the first stem portion is located at a 5' end of the RNA agent.

94. (previously presented): The agent of claim 90, wherein the first stem portion is located at a 3' end of the RNA agent.

95. (previously presented): The agent of claim 90, wherein the loop portion comprises at least 4 nucleotides.

96. (previously presented): The agent of claim 90, wherein the loop portion comprises at least 7 nucleotides.

97. (previously presented): The agent of claim 90, wherein the loop portion comprises 11 nucleotides.

98. (previously presented): The agent of claim 90, wherein the sequence of the mRNA is located in a 5' untranslated region (UTR) or a 3' UTR of the mRNA.

99. (previously presented): The agent of claim 90, wherein the first and second stem portions each comprise about 18 to about 30 nucleotides.

100. (previously presented): The agent of claim 90, wherein the first and second stem portions each comprise about 22 to about 28 nucleotides.

101. (previously presented): The agent of claim 90, wherein the first and second stem portions each comprise the same number of nucleotides.

102. (previously presented): The agent of claim 90, wherein one of the first and second stem portions comprises 1 to 4 more nucleotides than the other stem portion.

103. The agent of claim 90, wherein the target gene is a human gene.

104. (previously presented): The agent of claim 90, wherein the target gene is a mutant human gene.

105. (previously presented): The agent of claim 90, wherein the target gene is a viral gene.

106. (previously presented): A method of inducing ribonucleic acid interference (RNAi) of a target gene in a cell, the method comprising

i) obtaining a host cell of claim 87;

ii) culturing the cell; and

iii) enabling the cell to express the RNA agent to form a small interfering ribonucleic acid (siRNA) within the cell, thereby inducing RNAi of the target gene in the cell.

107. (New) A multitarget partially double-stranded RNA molecule comprising two or more different double stranded RNA sequences that are substantially homologous and complementary to two or more sequences of at least one target gene.

108. (New) The multitarget partially double-stranded RNA molecule of claim 107, wherein said two or more different double stranded RNA sequences are substantially homologous and complementary to two or more sequences of more than one target gene.

109. (New) The multitarget partially double-stranded RNA molecule of claim 107, wherein at least 11 to 30 nucleotides of said multitarget partially double-stranded RNA molecule are involved in each different double-stranded sequence.

110. (New) The multitarget partially double-stranded RNA molecule of claim 107, wherein each different double stranded RNA sequence comprises at least one segment of 30 contiguous nucleotides with a homology of at least 50% to a similar 30 nucleotide region of the target sequence, wherein said segment of 30 contiguous nucleotides is also non-homologous to any naturally occurring and essential polynucleotide sequence.

111. (New) The multitarget partially double-stranded RNA molecule of claim 107, wherein said multitarget partially double-stranded RNA molecule is between about 100 and 10,000 polynucleotides in length.

112. (New) The multitarget partially double-stranded RNA molecule of claim 107, wherein said multitarget partially double-stranded RNA molecule is at least about 200 nucleotides in length.

113. (New) The multitarget partially double-stranded RNA molecule of claim 107, wherein one or more of said different double stranded RNA sequences comprises a sense polynucleotide and an antisense polynucleotide separated by a non-base-paired polynucleotide sequence.

114. (New) The multitarget partially double-stranded RNA molecule of claim 113, wherein said sense and antisense polynucleotides form a hairpin.

115. (New) The multitarget partially double-stranded RNA molecule of claim 107, wherein said two or more different double stranded RNA sequences are separated by cleavage sequences.

116. (New) The multitarget partially double-stranded RNA molecule of claim 115, wherein said cleavage sequences are autocatalytic sequences or splice sites.

117. (New) The multitarget partially double-stranded RNA molecule of claim 107, wherein said at least one target gene is from a single target pathogen.

118. (New) The multitarget partially double-stranded RNA molecule of claim 69, wherein said more than one target genes are from more than one target pathogens.

119. (New) The multitarget partially double-stranded RNA molecule of claim 117, wherein said target pathogen is a virus.

120. (New) The multitarget partially double-stranded RNA molecule of claim 119, wherein said virus is selected from the group consisting of HBV, HIV, HSV, CMV, HPV, HTLV and EBV.

121. (New) The multitarget partially double-stranded RNA molecule of claim 118, wherein said more than one target pathogens are viruses.

122. (New) The multitarget partially double-stranded RNA molecule of claim 121, wherein said more than one viruses are selected from the group consisting of HBV, HIV, HSV, CMV, HPV, HTLV and EBV.

123. (New) The multitarget partially double-stranded RNA molecule of claim 107, wherein said at least one target gene is associated with a disease or disorder in a mammal.

124. (New) The multitarget partially double-stranded RNA molecule of claim 123, wherein said at least one target gene is a cancer-associated gene.

125. (New) The multitarget partially double-stranded RNA molecule of claim 108, wherein said more than one target genes are associated with a disease or disorder in a mammal.

126. (New) The multitarget partially double-stranded RNA molecule of claim 125, wherein said more than one target genes are cancer-associated genes.

127. (New) The multitarget partially double-stranded RNA molecule of claim 107, wherein said two or more sequences of said at least one target gene are selected from the group consisting of transcribed sequences, non-transcribed

sequences, coding sequences, non-coding sequences, exon-containing sequences, regulatory sequences and promoter sequences.

128. (New) The multitarget partially double-stranded RNA molecule of claim 107, wherein said multitarget partially double-stranded RNA molecule lacks a poly-adenylation signal.

129. (New) A composition comprising the multitarget partially double-stranded RNA molecule of claim 107.

130. (New) The composition of claim 129 further comprising an agent which facilitates polynucleotide uptake by a cell.

131. (New) A DNA molecule encoding the multitarget partially double-stranded RNA molecule of claim 107.

132. (New) An expression vector encoding the multitarget partially double-stranded RNA molecule of claim 107.

133. (New) The expression vector of claim 132, wherein said multitarget partially double-stranded RNA molecule is expressed using a promoter selected from the group consisting of a mitochondrial promoter, a RNA pol I promoter, a RNA pol II promoter, a RNA pol III promoter, a viral promoter, a bacterial promoter and a bacteriophage promoter.

134. (New) The expression vector of claim 133, wherein said multitarget partially double-stranded RNA molecule is expressed using a RNA pol III promoter.

135. (New) The expression vector of claim 132, wherein said vector is a plasmid, phage or recombinant virus.

136. (New) The expression vector of claim 132, wherein said encoded multitarget partially double-stranded RNA molecule lacks a poly-adenylation signal.

137. (New) An expression vector for reducing or inhibiting the function of at least one target gene in a cell, wherein said expression vector encodes two or more different double stranded RNA sequences that are homologous and complementary to two or more sequences of said at least one target gene.

138. (New) The expression vector of claim 137 wherein said two or more different double stranded RNA sequences are homologous and complementary to two or more target sequences of more than one target gene.

139. (New) The expression vector of claim 137, wherein each different double stranded RNA sequence comprises at least 11 to 30 nucleotides involved in the double-stranded sequence.

140. (New) The expression vector of claim 137, wherein each different double-stranded RNA sequence contains at least one segment of 30 contiguous nucleotides with a homology of at least 50% to a similar 30 nucleotide region of the target

sequence, wherein said segment of 30 contiguous nucleotides is also non-homologous to any naturally occurring and essential polynucleotide sequence in said cell.

141. (New) The expression vector of claim 137, wherein said vector encodes a multitarget partially double-stranded RNA molecule comprising two or more different double stranded RNA sequences.

142. (New) The expression vector of claim 141, wherein said multitarget partially double-stranded RNA molecule is between about 100 and 10,000 polynucleotides in length.

143. (New) The expression vector of claim 141, wherein said multitarget partially double-stranded RNA molecule is at least about 200 nucleotides in length.

144. (New) The expression vector of claim 137, wherein one or more of said different double stranded RNA sequences comprises a sense polynucleotide and an antisense polynucleotide separated by a non-base-paired polynucleotide sequence.

145. (New) The expression vector of claim 144, wherein said sense and antisense polynucleotides form a hairpin.

146. (New) The expression vector of claim 141, wherein said two or more different double stranded RNA sequences are separated by cleavage sequences.

147. (New) The expression vector of claim 146, wherein said cleavage sequences are autocatalytic sequences or splice sites.

148. (New) The expression vector of claim 137, wherein said two or more different double stranded RNA sequences are expressed using a promoter selected from the group consisting of a mitochondrial promoter, a RNA pol I promoter, a RNA pol II promoter, a RNA pol III promoter, a viral promoter, a bacterial promoter and a bacteriophage promoter.

149. (New) The expression vector of claim 148, wherein said one or more promoters are RNA pol III promoters.

150. (New) The expression vector of claim 137, wherein said two or more different double stranded RNA sequences are expressed using two or more promoters.

151. (New) The expression vector of claim 144, wherein said two or more different double stranded RNA sequences are expressed using two or more promoters.

152. (New) The expression vector of claim 150, wherein said two or more promoters are selected from the group consisting of a mitochondrial promoter, a RNA pol I promoter, a RNA pol II promoter, a RNA pol III promoter, a viral promoter, a bacterial promoter and a bacteriophage promoter.

153. (New) The expression vector of claim 152, wherein said two or more promoters are RNA pol III promoters.

154. (New) The expression vector of claim 151, wherein said two or more promoters are selected from the group consisting of a mitochondrial promoter, a RNA pol I promoter, a RNA pol II promoter, a RNA pol III promoter, a viral promoter, a bacterial promoter and a bacteriophage promoter.

155. (New) The expression vector of claim 154, wherein said two or more promoters are RNA pol III promoters.

156. (New) The expression vector of claim 137, wherein said vector is a plasmid, phage or recombinant virus.

157. (New) The expression vector of claim 137, wherein said at least one target gene is from a single target pathogen.

158. (New) The expression vector of claim 138, wherein said more than one target genes are from more than one target pathogens.

159. (New) The expression vector of claim 157, wherein said target pathogen is a virus.

160. (New) The expression vector of claim 159, wherein said virus is selected from the group consisting of HBV, HIV, HSV, CMV, HPV, HTLV and EBV.

161. (New) The expression vector of claim 158, wherein said more than one target pathogens are viruses.

162. (New) The expression vector of claim 161, wherein said more than one viruses selected from the group consisting of HBV, HIV, HSV, CMV, HPV, HTLV and EBV.

163. (New) The expression vector of claim 137, wherein said at least one target gene is associated with a disease or disorder in a mammal.)

164. (New) The expression vector of claim 163, wherein said at least one target gene is a cancer-associated gene.

165. (New) The expression vector of claim 138, wherein said more than one target genes are associated with a disease or disorder in a mammal.

166. (New) The expression vector of claim 165, wherein said more than one target genes are cancer-associated genes.

167. (New) The expression vector of claim 137, wherein said two or more sequences of said at least one target gene are selected from the group consisting of transcribed sequences, non-transcribed sequences, coding sequences, non-coding sequences, exon-containing sequences, regulatory sequences and promoter sequences.

168. (New) The expression vector of claim 137, wherein said two or more different double stranded RNA sequences lack a poly-adenylation signal.

169. (New) A method of making a composition comprising two or more different double stranded RNA molecules comprising expressing the expression vector of claim 137 in a cell.

170. (New) The composition comprising two or more different double stranded RNA molecules produced by the method of claim 169.

171. (New) A multitarget partially double-stranded RNA molecule encoded by the expression vector of claim 137.

172. (New) A composition comprising the expression vector of claim 137.

173. (New) The composition of claim 172 further comprising an agent which facilitates polynucleotide uptake by a cell.